COMPARISON OF ROLE OF SERUM- ASCITES ALBUMIN GRADIENT AND ASCITIC FLUID TOTAL PROTEIN IN LIVER CIRRHOSIS PATIENTS

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ABSTRACT

Objective: To compare the diagnostic sensitivity of serum/ ascites albumin gradient and ascitic fluid total protein in liver cirrhosis patients, using ultrasosnography as gold standard.

Study Design: Validation Study.

Place and duration of Study: Department of Chemical Pathology and Endocrinology, Armed Forces Institute of Pathology, Rawalpindi and Department of Radiology CMH/ MH Rawalpindi from 15 Jul 2007 to 15 May 2008.

Material and Method: Seventy three patients of liver cirrhosis were enrolled in the study by non-probability convenience sampling. Liver cirrhosis was confirmed on ultrasound abdomen. Ascitic fluid and 3 ml of blood were obtained simultaneously for analysis of serum albumin, ascitic fluid albumin & total proteins. Sensitivity of serum ascitic albumen gradient (SAAG) and serum ascitic fluid total protein (AFTP) was calculated by comparing with liver ultrasonographic findings (gold standard).

Results: Among 73 patients, 52 (71%) were males and 21 (29%) females. Mean ages was 57 years. Age range was 30-80 years. It was observed that sensitivity of SAAG in liver cirrhosis was 97% and that of AFTP was 53% only.

Conclusion: Diagnostic sensitivity of SAAG in liver cirrhosis is significantly higher than AFTP in workup of ascites related to portal hypertension.

Keywords: Albumin Gradient, cirrhosis, serum ascitic albumin

INTRODUCTION

Liver cirrhosis is defined anatomically as diffuse fibrosis with nodular hepatocyte regeneration[1]. The term "ascites" denotes to pathologic accumulation of fluid in the peritoneal cavity. Ascites is one of the earliest and common complications of chronic liver disease (CLD)[2]. Approximately 50% patients with compensated cirrhosis may develop ascites over a period of 10 years. This occurrence is an ominous sign in the natural history of end-stage liver disease because only 50% of patients survive 2 to 5 years after its onset[3]. The underlying mechanism for development of ascites is portal hypertension secondary to CLD, which accounts for more than 80% of patients with ascites[4].

The traditional classification of ascites is based on estimation of ascitic fluid total protein (AFTP), which is high (≥ 25 g/l) in exudate and low (< 25 g/l) in transudate[5]. This classification however has a limitation to correctly identify the aetiological and pathophysiological factors involved in development of ascites[6] and has been challenged in different clinical conditions especially in cirrhotic patients on prolonged diuretic therapy[7] and cases of bacterial peritonitis[8]. These drawbacks led to development of a new approach to classify ascites, based on serum ascites albumin gradient (SAAG) which is being used to differentiate ascitic fluid into two categories: first with gradient > 11 g/l in cases with portal hypertension and second with gradient <11 g/l in ascites unrelated to portal hypertension[9]. The superiority of SAAG to differentiate the ascites and to assess presence and degree of esophageal varices is well established[10-14].

SAAG is calculated by subtracting the ascitic fluid albumin from the serum albumin. It is to be noted that SAAG is not a ratio but a subtraction.

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SAAG (g/l) = Serum Albumin (g/l) – Ascitic fluid albumin (g/l)

Presently SAAG is not being used in our clinical practice, so this study was designed to compare the diagnostic sensitivity of SAAG and AFTP in ascites related to liver cirrhosis patients.

MATERIALS AND METHOD

This was a cross sectional comparative study carried out at the Department of Chemical Pathology& Endocrinology, Armed Forces Institute of pathology, Rawalpindi and Department of Radiology CMH/ MH Rawalpindi from 15 Jun 2007 to 15 May 2008. Seventy eight patients of ascites were interviewed who reported for ascitic fluid analysis by non-probability convenience sampling irrespective of sex and age. Five cases were excluded from the study on the basis ultrasonographic findings. Seventy three cases were included in the study. Written informed consent was obtained. Ultrasonography of liver was arranged at established centres. Standard ultrasonographic criteria of liver cirrhosis was used[15,16]. Simultaneously 3 ml of blood was collected aseptically in plain test tubes in lying posture. Application of torniquette was avoided or minimized to 30 seconds to avoid the effect of haemoconcentration. History and clinical examination of patients was carried out at the same time. Blood was allowed to clot and serum was separated. Estimation of albumin (g/l) was done on both serum and ascitic fluid by the Bromocresol green method[17] and AFTP (g/l) was estimated by Biuret method[18] on automated chemistry analyzer.

Statistical analysis of data was done by using statistical programme for social sciences (SPSS) version 11.0. Variables in the study were SAAG and AFTP. Sensitivity of SAAG and AFTP was calculated by comparing with ultrasonographic findings (gold standard) Sensitivity % = TP / TP + FN x 100. Statistical significance of the results of SAAG and AFTP was determined by applying Fisher's Exact Test.

RESULTS

Among 73 patients, 52 (71%) were males and 21 (29%) were females. Mean age was 57 years. Age range was 30 to 80 years. Results of SAAG and AFTP are shown in Table.1. Out of 73 patients, 71 (97%) were correctly identified as liver cirrhosis by SAAG at ≥ 11 g/l while only 39 (53%) patients were correctly identified as cases of liver cirrhosis (transudate) at AFTP < 25 g/l ($p<0.001$). Diagnostic sensitivities of SAAG and AFTP were 97% and 53% respectively.

DISCUSSION

Diagnostic paracentesis became increasingly important over the last two decades as the key initial test in the assessment of the ascitic patient. The traditional classification of ascites into 'exudative' and 'transudative' based on AFTP has been used since long. However, certain drawbacks led to a new approach to classify ascites, based on SAAG. As albumin is the main contributor of plasma oncotic pressure, so SAAG was measured as a reflection of portal hypertension in the genesis of ascites from liver cirrhosis.

Results of present study have shown that a majority of the patients belonged to older age group (mean age: 57 years), this can be explained by the finding that liver cirrhosis adopts a chronic and progressive spectrum[19]. In our study 52 patients (71%) were males, and this male predominance can be explained by the fact that males are more exposed to risk factors[21].

Results of the present study have also shown that AFTP at a cut off point of < 25 g/l has a sensitivity of 53 % to label ascites of hepatic origin. The various studies conducted world wide though did not measure sensitivity

Table: Results of SAAG in comparison to AFTP (n=73)

Study Parameters	Mean	SD	Range	p-value	Sensitivity %
SAAG (g/l)	19.0	4.3	7-30	<.001	97
AFTP (g/l)	22.4	7.4	6-40	<.001	53

but have shown poor accuracy of AFTP for discriminating ascites of hepatic origin (Table-2). In most of these studies diagnostic accuracy of AFTP is < 70% in comparison to the SAAG whose accuracy is well above 90%. Beg M et al reported sensitivity of AFTP as 65% for classifying ascites. Thus it is evident that results of our study are in agreement with studies conducted worldwide. On the other hand 47% of patients showed high AFTP values (>25 g/l) which could not be identified. Thus it can be said that AFTP is a poor predictor of ascites of hepatic origin.

In the study more the SSAG values were >11g/l (sensitivity=97%) as expected in liver cirrhosis. Mean value of SSAG was 19 g/l which was in accordance with Demyrel & Al-Knawy who reported mean SAAG (21 & 17g/l) respectively[20,21]. The possible reason for higher SAAG may be that disease was quite advanced at the stage which has led to significant portal hypertension. This fact is further consolidated by the finding that majority of the patients belonged to older age. Only two cases had SAAG <11g/l and simultaneously both cases had raised AFTP (exudate). These cases were even not identified by AFTP as well. So the results of this study show that SAAG is a useful diagnostic marker for the differentiation of ascites related to liver cirrhosis.

Manystudieshavecomparedtheroleof SAAG and AFTP in work-up of ascites, however, these studies had included all the cases of ascites instead of liver cirrhosis only as in present study.

These studies have demonstrated superiority of the SAAG in classifying ascites compared to transudate-exudate concept as proved by the present study. SAAG is a rapid, cost effective, non-invasive, and easily reproducible test whose accuracy is comparable to that of more invasive procedures like peritoneoscopy and biopsy[22, 23].

To summarize our results demonstrate that the SAAG is ≥11 g/l in 97% cases of liver cirrhosis patients with presumed portal hypertension. The results are similar to earlier studies with accuracy ranging from 91 to 100%[24-30].

CONCLUSION

Diagnostic sensitivity of SAAG in liver cirrhosis is significantly higher than AFTP in workup of ascites related to portal hypertension. So SAAG should replace transudative- exudative concept in differentiation of ascites.

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